

Disclaimer: These notes were taken by Ruth Dameron at the LMBBS Conference in Houston, June 17, 2006. There has been no attempt to verify accuracy. Do not quote the speakers based on these notes!

This was the Question/Answer time after all of the doctors had spoken. Dr. Richard Lewis, Cullen Eye Institute, Baylor College of Medicine, and Dr. Nico Katsanis, Johns Hopkins University, were present to answer questions.

(Note to reader: Ignore the annotation of the form “Axx” such as “A11”.)

Dr. Lewis recounted the story of the **Vitamin A recommendation**. In short: the study was flawed and it bears NO relevance to BBS. You cannot extrapolate their results to BBS. And their results may have been incorrectly reported.

Autism or autistic-like behaviors – hasn’t been studied extensively with BBS. [RHD note: I read one paper of a study re children with BBS in Newfoundland. I don’t recall the details but a significant number were rated with mild to moderate autism.] It’s a problem to define it. It needs to be studied. Is there a necessary correlation? We don’t know.

The definition of autism is not descriptive. It is more a broad spectrum of symptoms. Dr. Nico says, “I would prefer to dissect the components of BBS and report on them individually because they are quantitative and you can measure them. If you put a broader autism-like thing in the medical definition of BBS, you don’t learn anything additional. I propose you let us break down the various sensory issues we are dealing with; let’s put a label on the individual items and move on to other sensory issues. For example, anosmia (inability or reduced ability to smell) should be added to the list of BBS characteristics as also poor thermal sensation. [RHD note: In a panel session, parents still reiterated that using the phrase “autistic-like tendencies” communicates very well to teachers and other lay people what to expect re behavior even if such a broad phrase does not add to the specifics of a medical definition.]

What about the retina chips (Chicago, the Chao brothers, USC, the German chip ...)? Dr. Lewis responded as follows. the blunt answer is: Re the Chicago chip, the distributed and publically spoken information is very positive but there is no actual evidence that it’s true. Your retina has 125,000,000 sensors. The chips don’t recognize form (face, flower, etc.) or color or texture; depending on the array, they can in certain limited individuals detect motion. The retinal prostheses are nowhere even close to helping vision in the same way cochlear implants help hearing and the implants have been under development for over 20 years. Optobionics is very heavily touted since the “20/20” TV story. I’m not being negative. I’m being pragmatic. It doesn’t YET pass the “my mother, my brother” test. That is, I would not recommend it for my mother or my brother and therefore I won’t recommend it for anyone else (YET).

Dr. Nico said: In BBS patients, BBS proteins are lacking or defective. It’s much easier to stop a protein from being produced than it is to START it to be produced or improve its production. Blocking production is easier than stimulating production. This is why I’m most optimistic about the kidney – even if we have some drugs that would be toxic in your heart, it can be a very low dose

but the kidney will concentrate it and it could become a proper dose by the time it reached the kidney.

 Dr. Nico on Herschsprung's – During fetal development, neurons migrate from a specific area and populate the gut. We now think this movement of nerves is delayed or inhibited in BBS in the same mechanism as in Herschsprung's. The result is not enough nerves are present in the gut. Surgery is completely or partially successful. The proteins that cause Herschsprung's and the BBS genes interact to help orchestrate the movement of these nerves. There is a gene that is called RET. Mutations in RET are one of the things traditionally tested for Herschsprung's. 50% of patients with Herschsprung's were thought to have a mutation in RET but, until recently, the mutation had never been found. Genes carry the instruction to build a protein and the instruction to regulate WHEN to build the protein. In the last year, a new mutation has been found in RET that regulates its activity. This is not part of the traditional spectrum of mutations. This accounts for 50% of Herschsprung's patients. This is ALWAYS present in BBS patients with Herschsprung's symptoms. [RHD: Main point: the common test for Herschsprung's with respect to the RET gene does not currently test for the mutation that regulates when to build the protein. This is the one that is always present in BBS patients. Therefore you may be “tested for Herschsprung's” and be misdiagnosed as not having it.

 katsanis@jhmi.edu is Nico's email address. **Contact him if your child has Herschsprung's** – he needs to know in order to do certain research. Please do NOT contact him just to ask general questions. “I need to be in the lab. YOU want me to be in the lab, too.”

What about retina transplants? Traditionally the eye is viewed as an extension of the brain. Now we realize that the photosensor is older – you might think of the brain as an extension of the eye. In any case, the optic nerve has soooooo many fibers in such a small space and NO ONE knows how to connect them to the retina. No one.

What is the current status of stem cell research?

Nico answered apologized re his level of emotion. He is upset that there is an unnecessary political and emotional flareup regarding the value of stem cells. “Right now, we don't know what they are, how they work, how they differentiate, and whether it's safe to put them into humans.”

Lewis: we gave away the embryonic stem cell research to other countries when we limited it here. Someone in the audience asked what difference it makes as long as the research is happening. Dr. Lewis said there are many more researchers available in the U.S. to work on the problem if it were ok.

to donate blood of persons known to have BBS to the BBS research data bank:

Contact rlewis@bcm.edu or call 713-798-3030

 Has there been a study of the **long term psychological effects** on the child for whom there has been severe restriction and control of eating? No.

Cystic fibrosis has a **biochemical test and a molecular test**. If both test positive, it's for sure. If only one, it's less clear. It's very good when you can have both kinds of tests for a syndrome like BBS.

In BBS, we think, we will be able to use a biochemical assay on a skin sample to look at BBS and maybe point to which BBS gene, before doing a molecular test.

Nico will need to have skin samples, taken with anesthetic. If some are willing, send Nico Katsanis an email. (See comment below regarding cost. Nico cannot reimburse you for the expense. This would be your donation to science. Because it's for research, the place you have it done MIGHT be willing to charge less ... you can ask.) It MUST be delivered very rapidly, cannot take 2 days like blood to travel and still be useful. Should be delivered within 1 day. This is quite possible. For example, an afternoon sample can be FedExed for delivery the next morning. If we can't get enough skin samples, we might be able to take a **gallon** of urine from which to extract cells from the wall of the bladder.

Nominal charge for a skin biopsy is \$110. Some want to charge \$4,700! Be cautious.

Ideal research situation is to have skin samples from each of the BBS categories so we are sure that the screening we develop works for all types.

Nico discovered that BBS patients lack the sensory receptors to differentiate between normal temperature and a high temperature, unless it is MUCH higher.

For those of you willing to participate in the **temperature test** – it will probably take an hour or two in a neurologist office. Identify the neurologist that you know and trust who specializes in sensory perception. Contact Nico and HE will get in touch with the neurologist. He needs to be sure the same test is run in each case. Again, Nico's research budget is unable to reimburse you for the cost. Someone asked "What about cold?" Nico said he didn't no, had not tested that. He had tested heat with mice's tails. Some parents in the audience said their child could not detect cold.

Is there a relationship between **Prader-Willi and BBS**? Yes, there are two related proteins that interact but HOW they interact, etc., we don't know.

Hyperphagia – eating without an off-switch – where is it? In the brain, in the gut, in the muscle? If you never get a sensation of being "full", either 1) you don't recognize how much energy you are expending (muscle), 2) you don't recognize how much energy you are putting in (gut), or 3) the hypothalamus is not working right (brain). We don't know which of these is affected by BBS or if it is a combination.